

a<sup>1</sup>  
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isolated and purified DNA which hybridizes at high stringency conditions to the antisense complement of the urocortin II DNA under high stringency conditions (defined as membrane washing at high temperature and low salt concentration functionally equivalent to 0.1 x SSC at 65°C). Finally, the DNA may be an isolated and purified DNA encoding urocortin II but which differs in sequence due to the degeneracy of the genetic code. This DNA will preferably encode a protein of amino acid sequence SEQ ID No: 10 or amino acid SEQ ID NO: 11.

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Please replace the paragraph beginning at page 33, line 13, with the following rewritten paragraph:

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a<sup>2</sup>  
The instant invention is also directed to a vector capable of expressing the urocortin II. Such a vector consists of DNA encoding urocortin II and regulatory elements necessary for expression of urocortin II in a cell. In a preferred embodiment, this vector encodes a protein of amino acid sequence SEQ ID No: 10 or amino acid SEQ ID NO: 11. The instant invention is also directed to a host cell transfected with and expressing an urocortin II from such a vector. The protein may be expressed in a cell type selected from

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bacterial cells, mammalian cells, plant cells and insect cells. In a preferred embodiment, the protein is expressed in *E. coli*.

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Please replace the paragraph beginning at page 34, line 3, with the following rewritten paragraph:

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The instant invention is also directed to an isolated and purified urocortin II protein encoded from DNA as described above. Preferably, the purified urocortin II has an amino acid sequence corresponding to SEQ ID No: 10 or SEQ ID NO: 11.

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Please replace the paragraph beginning at page 34, line 16, with the following rewritten paragraph:

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The current invention is also directed to a DNA sequence encoding human urocortin-related peptide. This sequence may be an isolated and purified DNA that encodes human urocortin-related peptide. Alternatively, it may be an isolated and purified DNA which hybridizes at high stringency conditions to the antisense complement of the human urocortin-related peptide DNA under high stringency conditions (defined as membrane washing at high temperature and low salt concentration functionally equivalent to 0.1 x SSC at 65°C). Finally, the DNA may be an isolated and purified DNA encoding

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human urocortin-related peptide but which differs in sequence due to the degeneracy of the genetic code. This DNA will preferably have the sequence shown in SEQ ID No: 1 and will preferably encode a precursor protein of amino acid sequence SEQ ID No: 2 which is proteolytically processed to a protein of amino acid sequence SEQ ID NO: 3.

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Please replace the paragraph beginning at page 37, line 8, with the following rewritten paragraph:

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The instant invention is also directed to urocortin II or human urocortin-related peptide protein in which the standard "L-form" isomeric amino acids are replaced with "D-form" isomeric amino acids. In human urocortin-related protein, substitution of the isoleucine residue corresponding to position 9 of SEQ ID NO: 3 with D-isoleucine, D-phenylalanine, and D-Leucine or other D-form amino acids is particularly useful. Another useful substitution is the replacement of the glutamic acid residue at position 17 of SEQ ID NO: 3 or SEQ ID NO: 11 with D-glutamic acid.

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Please replace the paragraph beginning at page 39, line 13, with the following rewritten paragraph:

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In an effort to identify novel CRF-R ligands, a hidden Markov model (HMM) was constructed from a clustal W alignment of known CRF family proteins, including rat/human CRF, rat Ucn, human Ucn, frog sauvagine, and white-suckerfish urotensin I, using the HMMER software package (Sean Eddy, Department of Genetics, Washington University, St. Louis, MO; see ref. 19). This HMM was used to search the public human genome database and a BAC (Genbank accession no. AC005903) derived from chromosome 3p21.3-4 was identified that contained a 109 bp region exhibiting significant sequence homology but which was not a part of a previously identified gene. This region was extended to 621 bp with the identification of a human EST clone that overlapped with this sequence (Genbank accession No. BE622276). The human sequence, however, lacks a consensus proteolytic cleavage site that would allow for C-terminal processing of the peptide. Therefore, the protein was designated as a human urocortin-related peptide (hURP) sequence. Figure 1 shows the nucleotide (SEQ ID NO: 1) sequence of the predicted open reading frame of the human URP protein. This gene encodes a peptide of amino acid sequence SEQ ID NO: 2.

Please replace the paragraph beginning at page 41, line 10, with the following rewritten paragraph:

a<sup>7</sup> IVLSLDVPIGLLQILLEQARARAAREQATTNARIL  
ARVGH C-NH<sub>2</sub> (SEQ ID NO: 3).

Please replace the paragraph beginning at page 65, line 18, with the following rewritten paragraph:

a<sup>8</sup> Extensive analysis of other CRF receptor binding proteins has shown that substitution of normal amino acids with D-isomer amino acids or cyclizing amino acids results in increased affinity for CRF-receptors. In particular, an especially useful substitution is replacement of the isoleucine residue corresponding to position 9 of SEQ ID NO: 3 or SEQ ID NO: 11 with a "D-form" isomeric amino acid, preferably D-isoleucine, D-phenylalanine, and D-Leucine. Likewise, a glutamic acid residue corresponding to position 17 of SEQ ID NO: 3 or SEQ ID NO: 11 can be replaced with D-glutamic acid. Cyclizing amino acids can be formed by chemical bonds between the side chains of two or more residues. For example, adjacent glutamic acid and lysine residues can react to form an amide bond producing a lactam ring. Substitution with nonstandard amino acids such as C<sub>α</sub>-methylated leucine, C<sub>α</sub>-methylated alanine, N-im-benzylhistidine, 4-